

We claim:

1. A method for treating or preventing a CXCR4 mediated pathology comprising:
 - 5 administering a CXCR4 peptide antagonist to a host in an amount sufficient to inhibit CXCR4 signal transduction in a cell expressing a CXCR4 receptor or homologue thereof, wherein the CXCR4 peptide antagonist is not an antibody or fragment thereof.
 2. The method of claim 1, wherein the CXCR4 mediated pathology is cancer.
- 10 3. The method of claim 2, wherein the cancer is selected from the group consisting of bladder cancer, breast cancer, colorectal cancer, endometrial cancer, head & neck cancer, leukemia, lung cancer, lymphoma, melanoma, non-small-cell lung cancer, ovarian cancer, prostate cancer, testicular cancer, uterine cancer, cervical cancer, thyroid cancer, gastric cancer, brain stem glioma, cerebellar astrocytoma, 15 cerebral astrocytoma, ependymoma, Ewing's sarcoma family of tumors, germ cell tumor, extracranial cancer, Hodgkin's disease, leukemia, acute lymphoblastic leukemia, acute myeloid leukemia, liver cancer, medulloblastoma, neuroblastoma, brain tumors generally, non-Hodgkin's lymphoma, osteosarcoma, malignant fibrous histiocytoma of bone, retinoblastoma, rhabdomyosarcoma, soft tissue sarcomas generally, 20 supratentorial primitive neuroectodermal and pineal tumors, visual pathway and hypothalamic glioma, Wilms' tumor, acute lymphocytic leukemia, adult acute myeloid leukemia, adult non-Hodgkin's lymphoma, chronic lymphocytic leukemia, chronic myeloid leukemia, esophageal cancer, hairy cell leukemia, kidney cancer, multiple myeloma, oral cancer, pancreatic cancer, primary central nervous system lymphoma,

skin cancer, and small-cell lung cancer.

4. The method of claim 1, wherein the CXCR4 peptide antagonist is TN14003 or a derivative thereof.

5. The method of claim 1, wherein the CXCR4 peptide antagonist is selected from the group consisting of TC14012, and TE14011, or a combination thereof.

6. The method of claim 1, wherein the CXCR4 peptide antagonist inhibits signal transduction by interfering with ligand binding to a CXCR4 receptor or homologue thereof.

10 7. The method of claim 1, wherein the CXCR4 peptide antagonist specifically binds to CXCR4 receptors and thereby prevents SDF-1 α binding.

8. A method of treating cancer comprising administering to a host in need of such treatment a tumor-inhibiting amount of a CXCR4 peptide antagonist, a pharmaceutically acceptable salt or prodrug thereof, wherein the CXCR4 peptide 15 antagonist is not an antibody or antibody fragment.

9. The method of claim 8, wherein the cancer is selected from the group consisting of bladder cancer, breast cancer, colorectal cancer, endometrial cancer, head & neck cancer, leukemia, lung cancer, lymphoma, melanoma, non-small-cell lung cancer, ovarian cancer, prostate cancer, testicular cancer, uterine cancer, cervical 20 cancer, thyroid cancer, gastric cancer, brain stem glioma, cerebellar astrocytoma, cerebral astrocytoma, ependymoma, Ewing's sarcoma family of tumors, germ cell tumor, extracranial cancer, Hodgkin's disease, leukemia, acute lymphoblastic leukemia, acute myeloid leukemia, liver cancer, medulloblastoma, neuroblastoma, brain tumors generally, non-Hodgkin's lymphoma, osteosarcoma, malignant fibrous histiocytoma of

bone, retinoblastoma, rhabdomyosarcoma, soft tissue sarcomas generally, supratentorial primitive neuroectodermal and pineal tumors, visual pathway and hypothalamic glioma, Wilms' tumor, acute lymphocytic leukemia, adult acute myeloid leukemia, adult non-Hodgkin's lymphoma, chronic lymphocytic leukemia, chronic 5 myeloid leukemia, esophageal cancer, hairy cell leukemia, kidney cancer, multiple myeloma, oral cancer, pancreatic cancer, primary central nervous system lymphoma, skin cancer, and small-cell lung cancer.

10. The method of claim 8, wherein the peptide antagonist is TN14003 or a derivative thereof.

10 11. The method of claim 8, wherein the peptide antagonist is selected from the group consisting of T140, T22, TC14012, TE14011 or a combination thereof.

12. The method of claim 8, wherein the CXCR4 peptide antagonist inhibits tumor metastasis.

13. The method of claim 8, wherein the CXCR4 peptide antagonist 15 specifically binds to CXCR4 receptors and thereby prevents SDF-1 α binding.

14. A method for preventing tumor metastasis in a mammal comprising administering a metastasis inhibiting amount of a CXCR4 antagonist, a pharmaceutically acceptable salt, or prodrug thereof.

15. The method of claim 14, wherein the tumor is a cancer selected from the 20 group consisting of bladder cancer, breast cancer, colorectal cancer, endometrial cancer, head & neck cancer, leukemia, lung cancer, lymphoma, melanoma, non-small-cell lung cancer, ovarian cancer, prostate cancer, testicular cancer, uterine cancer, cervical cancer, thyroid cancer, gastric cancer, brain stem glioma, cerebellar astrocytoma, cerebral astrocytoma, ependymoma, Ewing's sarcoma family of tumors,

germ cell tumor, extracranial cancer, Hodgkin's disease, liver cancer, medulloblastoma, neuroblastoma, brain tumors generally, non-Hodgkin's lymphoma, osteosarcoma, malignant fibrous histiocytoma of bone, retinoblastoma, rhabdomyosarcoma, soft tissue sarcomas generally, supratentorial primitive neuroectodermal and pineal tumors, visual 5 pathway and hypothalamic glioma, Wilms' tumor, acute lymphocytic leukemia, adult acute myeloid leukemia, adult non-Hodgkin's lymphoma, esophageal cancer, kidney cancer, multiple myeloma, oral cancer, pancreatic cancer, primary central nervous system lymphoma, skin cancer, and small-cell lung cancer.

16. The method of claim 14, wherein the CXCR4 antagonist is TN14003 or a 10 derivative thereof.

17. The method of claim 14, wherein the CXCR4 antagonist is selected from the group consisting of TC14012 and TE14011 or a combination thereof.

18. The method of claim 14, wherein the CXCR4 antagonist inhibits tumor metastasis by interfering with ligand binding to a CXCR4 receptor or homologue thereof.

15 19. The method of claim 14, wherein the CXCR4 antagonist specifically binds to CXCR4 receptors and thereby prevents SDF-1 α binding.

20. A method for preventing tumor metastasis in a mammal comprising administering a metastasis inhibiting amount of a CXCR4 peptide antagonist, a pharmaceutically acceptable salt, or prodrug thereof, in combination with a second therapeutic agent, wherein the CXCR4 peptide antagonist is not an antibody.

21. The method of claim 20, wherein the tumor is a cancer selected from the group consisting of bladder cancer, breast cancer, colorectal cancer, endometrial cancer, head & neck cancer, leukemia, lung cancer, lymphoma, melanoma, non-small-cell lung cancer, ovarian cancer, prostate cancer, testicular cancer, uterine cancer,

cervical cancer, thyroid cancer, gastric cancer, brain stem glioma, cerebellar astrocytoma, cerebral astrocytoma, ependymoma, Ewing's sarcoma family of tumors, germ cell tumor, extracranial cancer, Hodgkin's disease, leukemia, acute lymphoblastic leukemia, acute myeloid leukemia, liver cancer, medulloblastoma, neuroblastoma, brain tumors generally, non-Hodgkin's lymphoma, osteosarcoma, malignant fibrous histiocytoma of bone, retinoblastoma, rhabdomyosarcoma, soft tissue sarcomas generally, supratentorial primitive neuroectodermal and pineal tumors, visual pathway and hypothalamic glioma, Wilms' tumor, acute lymphocytic leukemia, adult acute myeloid leukemia, adult non-Hodgkin's lymphoma, chronic lymphocytic leukemia, 10 chronic myeloid leukemia, esophageal cancer, hairy cell leukemia, kidney cancer, multiple myeloma, oral cancer, pancreatic cancer, primary central nervous system lymphoma, skin cancer, and small-cell lung cancer.

22. The method of claim 20, wherein the peptide antagonist is TN14003 or a derivative thereof.

15 23. The method of claim 20, wherein the peptide antagonist is selected from the group consisting of TC14012 and TE14011, or a combination thereof.

24. The method of claim 20, wherein the CXCR4 peptide antagonist inhibits signal transduction by interfering with ligand binding to a CXCR4 receptor or homologue thereof.

20 25. The method of claim 20, wherein the CXCR4 peptide antagonist specifically binds to CXCR4 receptors and thereby prevents SDF-1 α binding.

26. A method for detecting a cancer cell or cancer cell metastases comprising:

(a) contacting a cell sample with a CXCR4 antagonist comprising a

detectable label;

- (b) detecting the detectable label, and
- (c) correlating the amount of detectable label with the presence of cancer cells or cancer cell metastases.

5 27. The method of claim 26, wherein the CXCR4 antagonist is a peptide antagonist other than an antibody or antibody fragment.

28. The method of claim 27, wherein the CXCR4 peptide antagonist is TN14003.

29. The method of claim 27, wherein the CXCR4 peptide antagonist is 10 selected from the group consisting of TC14012 and TE14011.

30. A method for detecting a cancer cell or cancer cell metastases comprising:

- (a) contacting a cell sample with a fluorescently labeled CXCR4 peptide antagonist;
- (b) irradiating the cell sample comprising the fluorescently labeled CXCR4 peptide antagonist with an exciting amount of electromagnetic radiation;
- (c) detecting the emission of the fluorescently labeled CXCR4; and
- (d) correlating the detectable fluorescence with the presence of cancer cells or cancer cell metastases.

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31. A method for detecting a cancer cell or cancer cell metastases comprising:

- (a) contacting a cell sample with a biotinylated CXCR4 peptide antagonist;

- (b) contacting the cell sample comprising the biotinylated CXCR4 peptide antagonist with streptavidin conjugated detectable label;
- (c) detecting the detectable label; and
- (d) correlating the detectable label with the presence of cancer cells

5 or cancer cell metastases.

32. The method of claim 31, wherein the detectable label comprises a fluorophore or a radioisotope.

33. A method for inhibiting cancer metastasis comprising administering to a host in need of such treatment, a metastasis-inhibiting amount of CXCR4 polynucleotide 10 antagonist.

34. The method of claim 33, wherein the CXCR4 polynucleotide antagonist comprises an siRNA specific for a region of CXCR4 mRNA.

35. The method of claim 34, further comprising a second siRNA specific for a second region of CXCR4 mRNA.

15 36. A method for treating cancer comprising administering to a host in need of such treatment, a therapeutic amount of one or more siRNAs specific for CXCR4 mRNA or a fragment thereof.

37. A pharmaceutical composition comprising an siRNA specific for CXCR4 mRNA in an amount sufficient to inhibit tumor or cancer cell metastasis.

20 38. The composition of claim 37, wherein the siRNA comprises
UAAAAUCUUCCUGCCCACCDdTdT (SEQ ID NO: 15).

39. The composition of claim 37, wherein the siRNA comprises
GGAAGCUGUUGGCUGAAAAdTdT (SEQ ID NO: 16),

40. The composition of claim 37, comprising at least two siRNAs, wherein

each siRNA targets a different region of CXCR4 mRNA.

41. The method of claim 40, wherein the at least two siRNAs comprise
UAAAAUCUUCUCCUGCCCACCCdTdT (SEQ ID NO: 15) and
GGAAGCUGUUGGCUGAAAAdTdT (SEQ ID NO: 16).

5 42. A method of inhibiting tumor metastasis comprising administering to
a host in need thereof a pool of naked siRNAs, wherein the pool of naked siRNAs
comprise at least two siRNAs targeting different regions of CXCR4 mRNA.

43. The method of claim 42, wherein the siRNAs are conjugated to a
targeting substance.

10 44. The method of claim 43, wherein the targeting substance comprises
folate or a derivative thereof.

45. An siRNA conjugated to folate comprising a polynucleotide
sequence complementary to a region of CXCR4 mRNA, wherein said siRNA
inhibits tumor cell metastasis.

15 46. An extended release pharmaceutical composition comprising one or
more siRNAs specific for CXCR4 mRNA, a pharmaceutically acceptable salt, or
prodrug thereof and a means for controlled or delayed release.